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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/074,499
Filing Date: February 13, 2002
Appellant(s): ALOCILJA ET AL.

Ian C. McLeod
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed February 29, 2008 appealing from the Office action mailed September 4, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

- i) Kim et al. "Conductimetric membrane strip immunosensor with polyaniline-bound gold colloids as signal generator," *Biosensors & Bioelectronics*, vol. 14 (2000), pp.907-915.
- ii) US 5,958,791 ROBERTS et al. 9-1999

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 7-9, 14-16, 18-19, and 21 rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al (Biosensor & Bioelectronics (2000), vol. 14, pp. 907-915).

Kim et al. teach a conductimetric immunosensor substantially as claimed. The immunosensor (biosensor device) comprises:

a strip of a membrane (substrate) having at least two sections (zones) wherein a

(1) middle section (first of the zones) contains an antibody (first capture reagent) immobilized (bound) to the membrane (substrate) in a defined area between screen-printed thick film electrodes in an interdigitated structure, wherein the antibodies are immobilized on the interdigitated area comprising silver electrodes, wherein an anode and cathode are separated and the binding complex on the interdigitated structure is formed in between the electrodes (i.e. between electrodes on different sides of the defined area) (see page 911, right column, 1st full paragraph, lines 1-5; and Figure 3, and caption); and

(2) a lower section (second of the zones) containing a glass fiber membrane (fluid transfer medium) for sample application to the middle section (supplying a fluid to the first zone), wherein the lower section comprises a second defined area containing a second antibody (second capture reagent) that is directly bound to an electrically conductive polymer, i.e. polyaniline, or indirectly bound to the electrically conductive polymer through a colloidal gold particle, wherein the electrically conductive polymer, in the form of polyaniline, is created by a standard procedure of oxidative polymerization of aniline monomer in the presence of APS (i.e. polymer formed by oxidative polymerization of monomers) and the electrically conductive

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polymer has been mixed with the second antibody to form a conjugate, either with or without the colloidal gold particles (electrically conductive particles), wherein when a fluid sample containing an analyte is bound by the second antibody (capture reagent) to form a complex, the complex migrates to the middle section (first zone) of the membrane (medium) and the analyte is bound by the first antibody (capture reagent) thereby altering a conductivity of the defined area in the middle section as measured between the electrodes to detect the analyte (see pages 909-911; “Conclusions” on page 914; Figures 1 and 3-4, and captions).

Although Kim et al. teach that the preferred embodiment for the second antibody conjugate, which represents a labeling agent, comprises a colloidal gold-antibody conjugate that further includes the electrically conductive polymer on the surface thereof, Kim et al. do teach the “direct labeling” of the antibody with the electrically conductive polymer (see “Conclusions” section on page 914, the first 9 lines). Specifically, Kim et al. state, “This strategy for conductimetric detection could be a better approach than the **direct labeling of the antibody with the polymer...**”. This would indicate that such a direct labeling between the antibody and the conductive polymer was well known in the art at the time the invention was made. Therefore, it would have been obvious to utilize the “direct labeling” of the antibody with the electrically conductive polymer as disclosed by Kim et al. to achieve the predictable result of altering a conductivity of the measurement area between electrodes. Further, it would have reasonably been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of

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obvious design choice. *In re Leshin*, 125 USPQ 416. Additionally, all disclosures of non-preferred embodiments must be considered. 0126 USPQ 383, *In re Boe* 148 USPQ 507, *In re Lamberti et al.* 192 USPQ 278 (CCPA 1976).

With regards to claims 2, 9, and 15, Kim et al teach a cellulose membrane that is an absorption pad as an upper section of the immunosensor strip (i.e. third zone adjacent to the first zone). See Figures 1 and 3, and captions.

With regards to claims 16, 18-19, and 21, Kim et al teach microwells with sample medium into which the immunostrips were placed (i.e. third zone or pad is applied), as stated above. See page 909, 2nd full paragraph, lines 8-18; and Figure 1 and caption. Since the term “pad” has not been defined in the specification, the instant term is considered to be any substrate capable of containing a liquid sample medium.

With regards to claims 7 and 14, Kim et al also teach that voltage was applied across the electrodes (i.e. electrical means) and that conductimetric detection was performed by a conductivity meter, wherein the measurements can determine a transient response after complex formation between antigen and antibody (i.e. measuring means for determining a change in the conductivity of the first area between and after application of the sample). See page 910, left column, 1st paragraph, lines 5-8; and page 912, right column, 2nd full paragraph, lines 1-4.

Claims 3, 10, 22, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al (Biosensor & Bioelectronics (2000), vol. 14, pp. 907-915),

as applied to claims 1, 8, and 14 above, and further in view of Roberts et al (US 5,958,791).

The Kim et al. reference, which was discussed in the 103(a) rejection above, fails to teach a multiple array of first zones each having a first capture reagent with a different specificity to immobilize one of multiple analytes (claims 22, 24, and 26), and also fail to teach that the first defined area has a dimension between the electrodes of 1.0 mm (claims 3 and 10).

Roberts et al. teach a test device that includes multiple sets of interdigitated electrode arrays with an area of 6mm x 1mm, in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes (see column 18, lines 53-55; column 24, lines 1-6; and column 25, lines 16-20). In addition, Roberts et al. teach that the test device is a test strip with capillary flow through an absorbent material with a capture region, wherein the capture region contains binding material that can be an antibody (see column 5, lines 29-42 and 55-56; column 11, lines 29-40; and Figure 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kim et al. to include multiple sets of interdigitated electrode arrays with an area of 6mm x 1mm, as taught by Roberts et al., in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes. The electrode arrays of Roberts et al. have the advantage of allowing multiple tests to be performed at once, thereby cutting down on experimentation time, and providing motivation for combining the electrode arrays with

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the device of Kim et al. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including multiple sets of interdigitated electrode arrays with an area of 6mm x 1mm, as taught by Roberts et al., in the device of Kim et al., since Kim et al. teach a test strip with an antibody-layered capture region on an interdigitated electrode wherein sample can flow up the strip, and the interdigitated electrode arrays of Roberts et al. also include a capture region with immobilized antibody, and are on a test strip that can accommodate capillary flow.

In regards to claim 26, since Kim et al. and Roberts et al. in combination teach a device comprising an array of interdigitated electrodes, the intended use limitation "multiple analytes can be detected simultaneously from the sample by providing a constant current and measuring generated voltages across the area of each of the first zones" is fully capable of being performed by the device.

(10) Response to Argument

Applicant's arguments have been fully considered but they are not persuasive.

I. Applicant's first argument (see pages 11-20 of Appeal Brief) is with regard to the rejection of claims 1-2, 7-9, 14-16, 18-19, and 21 under 35 U.S.C. 103(a) as being unpatentable over Kim et al (Biosensor & Bioelectronics (2000), vol. 14, pp. 907-915). In particular, Applicant argues that a *prima facie* case of obviousness has not been established for modifying the Kim et al. reference so as to provide the claimed biosensor device because 1) there is no teaching or suggestion for the modification; and 2) Applicant believes Kim et al. actually teach *away* from the limitations claimed in the

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instant application. The statement in Kim et al. that Applicant points to for the "teaching away" of the reference is the following from page 914 of the reference (5. Conclusions):

"An additional labeling agent comprising a conducting polymer to colloidal gold-antibody conjugates facilitated electric conduction between gold particles captured via antigen-antibody binding. This strategy for conductimetric detection could be a better approach than the direct labeling of the antibody with the polymer by chemical reaction because, in such a case, the protein molecule itself does not contain available sites for electron relay. Therefore, the conductimetric gold tracer could provide a simple procedure for its preparation and also a new concept for quick, sensitive analysis based on immuno-chromatography for a number of clinical indicators, for examples, hormones, protein markers, and infectious organisms." (Emphasis Added).

Examiner agrees that the Kim et al. reference teaches the use of conductive gold particles, which are both conjugated to a binding member (i.e. antibody) specific for an analyte of interest and linked to a polymeric conductor molecule (i.e. polyaniline). The conjugated gold particles are used within an apparatus, similar to Applicant's, which includes a membrane strip having two sections, a middle and lower section. The middle section contains an antibody immobilized to the membrane in a defined area between two electrodes; and the lower section contains a membrane for sample application to the middle section, wherein the lower section includes a defined area comprising the conjugated gold particles (see Figures 1, 3 and 4 and captions; and pages 909-911).

Although Kim et al. rely on the gold particles in conjunction with the polymeric conductor molecule to provide an enhanced electric conduction (see pages 913-914), Kim et al. do teach the "direct labeling" of the antibody with the electrically conductive polymer (see "Conclusions" section on page 914, first 9 lines). The specific statement

of Kim et al. for the “direct labeling”, which Applicant also pointed to for the “teaching away”, is the following:

“This strategy for conductimetric detection could be a better approach than the direct labeling of the antibody with the polymer by chemical reaction...”

It is clear from the reference that the preferred embodiment of Kim et al. is the inclusion of the gold particles with the conductive polymeric molecules, however, the teaching by Kim et al. for the "direct labeling" of the antibody would indicate that such a direct labeling between the antibody and the conductive polymer was well known in the art at the time the invention was made. Therefore, it would have been obvious to utilize the “direct labeling” of the antibody with the electrically conductive polymer as disclosed by Kim et al. to achieve the predictable result of altering a conductivity of the measurement area between electrodes. Further, it would have reasonably been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 125 USPQ 416. Additionally, all disclosures of non-preferred embodiments must be considered. *In re Nehrenberg* 126 USPQ 383, *In re Boe* 148 USPQ 507, *In re Lamberti et al.* 192 USPQ 278 (CCPA 1976).

In addition, although Kim et al. provides an improvement to the electric conduction in a conductimetric immuno-chromatographic assay system by conjugating gold particles to a conductive polymeric molecule, the “direct labeling” of the antibody taught by Kim et al., which may be considered inferior, is merely an alternative and not a "teaching away." The statement (i.e. "Conclusions" section on page 914, first 9 lines)

of Kim et al. regarding the "direct labeling" of the antibody with the conductive polymer indicates that this "direct labeling" was well known in the art at the time of the invention. Because a "known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use," the "direct labeling" recited by Applicant's claimed invention should not be considered patentable over the prior art reference of Kim et al. (see MPEP § 2145; and *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)).

In conclusion, the rejection of claims 1-2, 7-9, 14-16, 18-19, and 21 under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Biosensor & Bioelectronics (2000), vol. 14, pp. 907-915) should be maintained because Kim et al. do provide a teaching of the "direct labeling" of the antibody, and the teaching should not be considered a "teaching away," but merely a known alternative.

II. Applicant's second argument (see pages 21-24 of Appeal Brief) is with regard to the rejection of claims 3, 10, 22, 24, and 26 under 35 U.S.C. 103(a) as being unpatentable over Kim et al (Biosensor & Bioelectronics (2000), vol. 14, pp. 907-915), as applied to claims 1, 8, and 14 above, and further in view of Roberts et al (US 5,958,791). In particular, Applicant argues that neither Kim et al. nor Roberts et al. teach a single multiple array for the detection of multiple analytes simultaneously from a single sample. Applicant points to the single multiple array illustrated in Figure 3 of the instant application, and argues that the simultaneous multiple analyte detection taught by Roberts et al. requires multiple sets of interdigitated electrode arrays.

Examiner agrees that the Kim et al. reference fails to teach a single multiple array for the detection of multiple analytes simultaneously, which is why the Kim et al. reference was combined with Roberts et al. However, Applicant's argument with respect to Roberts et al. is not found persuasive because the test device of Roberts et al. allows for the detection of multiple analytes simultaneously on a single strip of substrate.

The test device of Roberts et al. includes multiple set of interdigitated electrodes arrays in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes (see column 18, lines 53-55; column 24, lines 1-6; and column 25, lines 16-20). In addition, Roberts et al. teach that the test device is a test strip with capillary flow through an absorbent material with a capture region, wherein the capture region contains binding material that can be an antibody (see column 5, lines 29-42 and 55-56; column 11, lines 29-40; and Figure 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kim et al. to include multiple sets of interdigitated electrode arrays, as taught by Roberts et al., in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes. The electrode arrays of Roberts et al. have the advantage of allowing multiple tests to be performed at once, thereby cutting down on experimentation time, and providing motivation for combining the electrode arrays with the device of Kim et al. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including multiple sets of interdigitated electrode arrays, as taught by Roberts et al., in the device of Kim et al., since Kim et al.

teach a test strip with an antibody-layered capture region on an interdigitated electrode wherein sample can flow up the strip, and the interdigitated electrode arrays of Roberts et al. also include a capture region with immobilized antibody, and are on a test strip that can accommodate capillary flow.

Applicant's claims 22, 24 and 26, which recite on the multi-array device, require a plurality of first zones on the single strip of substrate, each with a first capture reagent bound to the single strip of substrate between electrodes to immobilize one of multiple analytes on the single strip of substrate so that each of the multiple analytes can be detected simultaneously. Therefore, the fact the Roberts et al. require multiple sets of interdigitated arrays is irrelevant given that the claims only require a single strip of substrate with multiple "first zones." Applicant points to their disclosure by referring to their embodiment of Figure 3 and how this embodiment differs from the teaching in Roberts et al. Although, it is appropriate to read a claim in light of the specification, it is inappropriate to import claim limitations from the specification. See MPEP § 211.01.

Further, Applicant appears to be arguing against the references individually, and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Therefore, the combination of Kim et al. in view of Roberts et al. should be maintained to reject claims 3, 10, 22, 24, and 26 of Applicant's instant invention because the combination results in the device lay-out of Kim et al., wherein multiple electrode arrays (i.e. first zones) are included on the single substrate strip in order to

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perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes, as taught by Roberts et al.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Examiner, Art Unit 1641

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